CLAIMS

1. A method of selection of a nucleic acid encoding an enzyme that is capable of converting a prodrug to its active drug form comprising the steps of:

a) contacting a population of bacteria transformed with a bacteriophage library with a prodrug in a medium, wherein;

i) the transformed bacteria are in the lysogenic state, and

ii) when converted to its active drug form, the prodrug causes activation of the proteolytic activity of bacterial RecA and lysis of the bacteria;

b) separating bacteriophage particles released by lysis of the bacteria from said medium, and

c) analysing the genotype of said separated bacteriophage for a nucleic acid encoding the enzyme.

2. A method for selection of a nucleic acid encoding an enzyme capable of converting a prodrug to its active drug form comprising the steps of:

a) introducing a library of genes into bacteriophage to form a bacteriophage library;

b) infecting a population of bacteria with said bacteriophage library;

c) selecting said infected bacteria for bacteria in which the lysogenic state has been established;

d) contacting said bacteria with said prodrug in a medium;

e) separating from said medium bacteriophage particles released by lysis of host bacteria; and

f) analysing the genotype of said selected bacteriaphage for the nucleic acid encoding the enzyme;

wherein said prodrug causes activation of the proteolytic activity of bacterial recA when converted to its active drug form.

3. A method according to claim 1 or claim 2 wherein said steps are repeated in at least one cycle.

4. A method according to any one of the preceding claims wherein the DNA sequence of said released bacteriophage particles is analysed.

5. A method according to any one of the preceding claims wherein said bacteriophage carry a gene encoding antibiotic resistance or other selectable marker.

6. A method according to any one of the preceding claims wherein said enzyme is nitroreductase, flavin reductase, DT-diaphorase, thymidine kinase, cytosine deaminase or a purine nucleoside phosphorylase.

7. A method according to any one of the preceding claims wherein said prodrug is CB1954, SN 23862, 2-[N,N-bis(2-iodoethyl)amino]-3,5-dinitrobenzamide 5-fluorocytosine, acyclovir, ganciclovir, or 6-methyl-9-(2-deoxy-β-D-erythro-pentofuranosyl) purine.

8. A method according to any one of the preceding claims wherein said temperate bacteriophage is the bacteriophage lambda or a lambda derivative.

9. A method according to any one of claims 2-8 wherein said gene library comprises genes encoding variants of a single enzyme.

10. A method according to claim 9 wherein said variants comprise amino acid deletions, insertions and substitutions from the wild type enzyme sequence.

11. A method according to claim 9 or 10 wherein said variants are generated by DNA shuffling, random mutagenesis, or PCR shuffling.

12. A method according to any one of the preceding claims wherein said activity of said bacterial RecA protein is caused by the generation of single-stranded DNA in the bacterium.

13. A method according to claim 12 wherein said single-stranded DNA is generated as a consequence of the enzymatic conversion of prodrug to its active drug form.

14. A method according to claim 13 wherein said single-stranded DNA arises as a result of a break in one or both strands of the DNA, a cytotoxic lesion, a DNA crosslink or a monovalent DNA adduct, or by inhibition of the progress of DNA replication by any other means.

15. A method according to any one of the preceding claims wherein said enzyme comprises nitroreductase and said prodrug comprises CB1954.

16. A method according to any one of the preceding claims wherein said bacteriophage vector is λJG3J1.

17. A method according to any one of the preceding claims wherein said bacterium is of the *E. coli* strain C600*Hfl*.

18. A catalytic enzyme or enzyme fragment isolated according to the method of any one of the preceding claims.

19. A nucleic acid molecule encoding a catalytic enzyme or enzyme fragment according to claim 18.